Protective effects of human iPS-derived retinal pigment epithelium cell transplantation in the retinal dystrophic rat.

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Public Summary:
Induced pluripotent stem (iPS) cells have the potential to differentiate into any cell type, making them a potential source from which to produce cells as a therapeutic platform for the treatment of a wide range of diseases. In many forms of human retinal disease, including age-related macular degeneration (AMD), the underlying pathogenesis resides within the support cells of the retina, the retinal pigment epithelium (RPE). As a monolayer of cells critical to photoreceptor function and survival, the RPE is an ideally accessible target for cellular therapy. Here we report the differentiation of human iPS cells into RPE. We found that differentiated iPS-RPE cells were morphologically similar to, and expressed numerous markers of developing and mature RPE cells. iPS-RPE are capable of phagocytosing photoreceptor material, in vitro and in vivo following transplantation into the Royal College of Surgeons (RCS) dystrophic rat. Our results demonstrate that iPS cells can be differentiated into functional iPS-RPE and that transplantation of these cells can facilitate the short-term maintenance of photoreceptors through phagocytosis of photoreceptor outer segments. Long-term visual function is maintained in this model of retinal disease even though the xenografted cells are eventually lost, suggesting a secondary protective host cellular response. These findings have identified an alternative source of replacement tissue for use in human retinal cellular therapies, and provide a new in vitro cellular model system in which to study RPE diseases affecting human patients. These cells might be a potential source for therapies to treat age-related macular degeneration.

Scientific Abstract:
Transformation of somatic cells with a set of embryonic transcription factors produces cells with the pluripotent properties of embryonic stem cells (ESCs). These induced pluripotent stem (iPS) cells have the potential to differentiate into any cell type, making them a potential source from which to produce cells as a therapeutic platform for the treatment of a wide range of diseases. In many forms of human retinal disease, including age-related macular degeneration (AMD), the underlying pathogenesis resides within the support cells of the retina, the retinal pigment epithelium (RPE). As a monolayer of cells critical to photoreceptor function and survival, the RPE is an ideally accessible target for cellular therapy. Here we report the differentiation of human iPS cells into RPE. We found that differentiated iPS-RPE cells were morphologically similar to, and expressed numerous markers of developing and mature RPE cells. iPS-RPE are capable of phagocytosing photoreceptor material, in vitro and in vivo following transplantation into the Royal College of Surgeons (RCS) dystrophic rat. Our results demonstrate that iPS cells can be differentiated into functional iPS-RPE and that transplantation of these cells can facilitate the short-term maintenance of photoreceptors through phagocytosis of photoreceptor outer segments. Long-term visual function is maintained in this model of retinal disease even though the xenografted cells are eventually lost, suggesting a secondary protective host cellular response. These findings have identified an alternative source of replacement tissue for use in human retinal cellular therapies, and provide a new in vitro cellular model system in which to study RPE diseases affecting human patients.